

WHAT IS CLAIMED IS:

Selection of D-able subsites

Claims 1-34. (Canceled).

Design of ZFPs using a Database

35. (Previously amended) A method of producing a zinc finger protein comprising:

- (a) providing a database comprising designations for a plurality of zinc finger proteins, each protein comprising at least first, second and third fingers, and subdesignations for each of the three fingers of each of the zinc finger proteins;  
a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising at least first, second and third triplets specifically bound by the at least first, second and third fingers respectively in each zinc finger protein, the first, second and third triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first, second and third fingers are arranged in the zinc finger protein (N-terminal to C-terminal);
- (b) providing a target site for design of a zinc finger protein, the target site comprising contiguous first, second and third triplets in a 3'-5' order,
- (c) for the first, second and third triplet in the target site, identifying first, second and third sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein(s) comprising a finger specifically binding to the second triplet in the target site, the third set comprising zinc finger protein(s) comprising a finger specifically binding to the third triplet in the target site;
- (d) outputting designations and subdesignations of the zinc finger proteins in the first, second, and third sets identified in step (c).

36. (Original) The method of claim 35, further comprising:

- (e) producing a zinc finger protein that binds to the target site comprising a first finger from a zinc finger protein from the first set, a second finger from a zinc finger protein from the second set, and a third finger from a zinc finger protein from the third set.

37. (Previously amended) The method of claim 36 further comprising identifying subsets of the first, second and third sets, the subset of the first set comprising zinc finger protein(s) comprising a finger that specifically binds to the first triplet in the target site from the first finger position of a zinc finger protein in the database; the subset of the second set comprising zinc finger protein(s) comprising a finger that specifically binds to the second triplet in the target site from the second finger position in a zinc finger protein in the database; the subset of the third set comprising zinc finger protein(s) comprising a finger that specifically binds to the third triplet in the target site from a third finger position in a zinc finger protein in the database;

wherein

the outputting step comprises outputting designations and subdesignations of the subset of the first, second and third sets; and

the producing step comprises producing a zinc finger protein comprising a first finger from the first subset, a second finger from the second subset, and a third finger from the third subset.

38. (Original) The method of claim 37, wherein the outputting comprises outputting the designations and subdesignations of the subsets of the first, second and third sets, and the first, second and third sets minus their respective subsets.

39. (Original) The method of claim 38, wherein each of the subsets is a null set.

40. (Original) The method of claim 35, wherein the target site is provided by user input.

41. (Previously amended) The method of claim 35 wherein the target site is provided by

providing a target nucleic acid to be targeted by a zinc finger protein;

selecting a plurality of potential target sites within the target nucleic acid sequence;

evaluating whether each selected target site comprises 5'NNx aNY bNzc3; and

outputting a selected target site within the target nucleic acid comprising 5'NNx aNy bNzc3', the output selected target site providing the target site in step (b) of claim 35,

wherein

each of (x, a), (y, b) and (z, c) is (N, N) or (G, K);  
 at least one of (x, a), (y, b) and (z, c) is (G, K). and  
 N and K are IUPAC-IUB ambiguity codes.

42. (Original) A method of producing a zinc finger protein comprising:
- (a) providing a database comprising
    - designations for a plurality of zinc finger proteins, each protein comprising at least first, and second fingers,
    - subdesignations for each of the fingers of each of the zinc finger proteins;
 and
    - a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising first and second triplets specifically bound by the first and second fingers respectively, the triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first and second fingers are arranged in the zinc finger protein (N-terminal to C-terminal);
  - (b) providing a target site for design of a zinc finger protein, the target site comprising contiguous first, and second triplets ordered 3'5' in the target site;
  - (c) for the first and second triplet in the target site, identifying first and second sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein comprising a finger specifically binding to the second triplet in the target site;
  - (d) outputting designations and subdesignations of the zinc finger proteins in the first, and second sets identified in step (c).

- 43 (Original) A method of producing a zinc finger protein comprising:
- (a) providing a database comprising:
    - designations for a plurality of zinc finger proteins, each protein comprising at least first, and second fingers;
    - subdesignations for each of the fingers of each of the zinc finger proteins;
 and

a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising first, and second triplets specifically bound by the first and second fingers respectively, the triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first and second fingers are arranged in the zinc finger protein (N-terminal to C-terminal);

(b) providing a target site for design of a zinc finger protein, the target site comprising contiguous first, second and third triplets ordered 3'5' in the target site;

(c) for the first and third triplet in the target site, identifying first and second sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising zinc finger protein comprising a finger specifically binding to the third triplet in the target site;

(d) outputting designations and subdesignations of the zinc finger proteins in the first, and second sets identified in step (c).

Claims 44-47 (Canceled).

48. (Amended) A computer program product for designing a zinc finger protein comprising:

(a) code for providing a database comprising

designations for a plurality of zinc finger proteins, each protein comprising at least first, second and third fingers ,

subdesignations for each of the three fingers of each of the zinc finger proteins;

a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising at least first, second and third triplets specifically bound by the at least first, second and third fingers respectively in each zinc finger protein, the first, second and third triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first, second and third fingers are arranged in the zinc finger protein (N-terminus to C-terminus);

(b) code for providing a target site for design of a zinc finger protein, the target site comprising at least first, second and third triplets,

- (c) for the first, second and third triplet in the target site, code for identifying first, second and third sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising a finger specifically binding to the second triplet in the target site, the third set comprising a finger specifically binding to the third triplet in the target site;
- (d) code for outputting designations and subdesignations of the zinc finger proteins in the first, second, and third sets identified in step (c).
- (e) a computer readable storage medium for holding the codes.

49. (Original) A system for designing a zinc finger protein comprising:

- (a) a memory;
- (b) a system bus;
- (c) a processor operatively disposed to:
  - (1) provide a database comprising designations for a plurality of zinc finger proteins, each protein comprising at least first, second and third fingers, subdesignations for each of the three fingers of each of the zinc finger proteins; a corresponding nucleic acid sequence for each zinc finger protein, each sequence comprising at least first, second and third triplets specifically bound by the at least first, second and third fingers respectively in each zinc finger protein, the first, second and third triplets being arranged in the nucleic acid sequence (3'-5') in the same respective order as the first, second and third fingers are arranged in the zinc finger protein (N-terminus to C-terminus);
  - (2) provide or be provided with a target site for design of a zinc finger protein, the target site comprising at least first, second and third triplets,
  - (3) for the first, second and third triplet in the target site, identifying first, second and third sets of zinc finger protein(s) in the database, the first set comprising zinc finger protein(s) comprising a finger specifically binding to the first triplet in the target site, the second set comprising a finger specifically binding to the second triplet in the target site, the third set comprising a finger specifically binding to the third triplet in the target site;
  - (4) output designations and subdesignations of the zinc finger proteins in the first, second, and third sets identified in step (3).

50. (Canceled)

51. (Canceled)

52. (Previously added) The method of claim 35 wherein the target site is provided by

providing a polynucleotide sequence;

selecting a potential target site within the polynucleotide sequence; the potential target site comprising contiguous first, second and third triplets of bases at first, second and third positions in the potential target site;

determining a plurality of subscores by applying a correspondence regime between triplets and triplet position in a sequence of three contiguous triplets, wherein each triplet has first, second and third corresponding positions, and each combination of triplet and triplet position has a particular subscore

calculating a score for the potential target site by combining subscores for the first, second, and third triplets;

repeating the selecting, determining and calculating steps at least once on a further potential target site comprising first, second and third triplets at first, second and third positions of the further potential target site to determine a further score;

providing output of at least one potential target site with its score, the at least one output potential target site providing the target site for step (b) in claim 35.